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A Clinical Study of the Iodoacetate Index (Huggins Test) in Cancer and in Various Nonmalignant Pathologic Conditions: Because the degree of the success of cancer therapy is directly related to the promptness of the diagnosis and of the institution of treatment, tests on blood and the body fluids that might aid in the diagnosis of cancer soon after its inception have been sought diligently. Huggins has recently reviewed the status and accomplishments in this field, and Huggins, Miller and Jensen have recently described 3 different tests that they utilized to study the heat coagulative capacity of the serum proteins in patients with cancer and in patients with miscellaneous nonmalignant pathologic conditions. These tests were "least concentration of heat coagulable protein," "iodoacetate index in relation to the serum albumin concentration," and the "iodoacetate index in relation to the serum total protein concentration."

These authors found by their test for "least concentration of coagulable protein" that in most of their patients with cancer and in some patients with certain nonmalignant pathologic conditions, including tuberculosis, a larger concentration of serum total protein was required for heat coagulation than was required in normal subjects. Huggins and Jensen found that iodoacetate inhibits the heat coagulation of serum proteins; from the largest concentration of iodoacetate in which serum coagulates, under the conditions of testing, and the concentration of albumin or of total protein in the serum, the "iodoacetate index in relation to the serum albumin concentration" and the "iodoacetate index in relation to the serum total protein concentration," respectively, were calculated. The data of Huggins and his associates on these tests showed lower iodoacetate indexes in relation to both serum albumin and total protein in most of their patients with cancer and in certain patients with nonmalignant pathologic conditions, including tuberculosis, than in normal subjects. From analyses of their data on these 3 tests, these authors concluded that "relating the iodoacetate index to the total protein content of the serum (the Huggins test) gave the most useful information."

The primary purpose of the present study was to gain additional information concerning the value of the Huggins test (iodoacetate index as related to the total serum protein) as a possible aid in the diagnosis of cancer. Accordingly, the test was employed in a series of normal subjects, patients with cancer and patients with a wide variety of nonmalignant pathologic conditions, and the results were then analyzed in relation to the clinical and pathological findings. In some cases the authors also studied in the same subjects the least concentration of heat-coagulable protein of the serum and the iodoacetate index as related to the serum albumin, both of these 2 additional tests being performed as described by Huggins et al. To investigate the effect of tissue damage and inflammation, and of blood loss on the iodoacetate index, the procedure was performed before and at varying intervals after surgical operations for cancer and for noncancerous lesions. The findings for the serum albumin and total protein concentrations in the patients with cancer were compared with those of the normal subjects studied. Also, in a small series of patients the sedimentation rate was studied in relation to the iodoacetate index.

The findings in a series of subjects in whom the 3 tests described by Huggins et al. were investigated confirm the results obtained by Huggins and his co-workers in the respect that the results in some patients with cancer and in other patients with many different nonmalignant pathologic conditions were widely different from those in normal persons. The data also demonstrated that the results of the iodoacetate index as related to the total protein concentration of the serum in normal subjects showed less overlapping of the results obtained in patients with cancer than the results of the test for the least concentration of heat-coagulable protein, or the iodoacetate index as related to the albumin concentration of the serum.

The findings in this study that only 39 (72 percent) of 54 patients with cancer had abnormally low iodoacetate indexes do not accord well with the findings of Huggins et al. that all of 85 consecutively studied patients with "clinically active" cancer showed abnormally low values. All 15 (28 percent) of the series of 54 patients who had normal iodoacetate indexes could certainly be considered as having "clinically active" cancer and many of them had large and inoperable tumors with evidences of metastases. This finding per se negated the hope that the Huggins test might afford a useful tool in the diagnosis of early cancer. The authors can offer no tenable explanation for the difference in the results of Huggins and his associates and the results in this study.

In the studies on preoperative patients with a wide variety of nonmalignant pathologic conditions, the incidence of "positive" values was 42 percent of 107 patients. That this incidence was so much higher than the 17 percent of "positive" tests obtained by Huggins et al. in 95 patients with nonmalignant conditions is of no real statistical significance, but rather depends on the kind and severity of the disease present at the time of study. Huggins and his co-workers pointed out that all of 7 patients with tuberculosis whom they studied showed "positive" iodoacetate indexes. As the studies progressed in this group with nonmalignant pathologic conditions, the authors at times deliberately selected patients with infections of widely varying types, ulcerative lesions, and so forth in whom they had learned to expect a high incidence of "positive" tests. Huggins and his associates have stressed that the iodoacetate index is nonspecific for cancer and this is unquestionably confirmed by the data in this study

The finding that the iodoacetate index is so frequently abnormally increased in a wide variety of infections, in ulcerative lesions, in inflammatory or necrotic processes, and in the presence of tissue damage after surgical operation raises the question whether the lowered index found in certain patients with cancer may not be related to inflammatory, necrotic or other changes in, or caused by, the tumor. It is presumed that changes in the plasma proteins, which alter the iodoacetate index, occur within the liver. That patients with cancer show a high incidence of hepatic dysfunction has been demonstrated by the results of Abels et al. in their studies of eight different tests for hepatic function in patients with gastro-intestinal cancer.

Because some of the patients with cancer in whom studies of the iodoacetate index were made at the outset of this investigation had undergone major operations a few days before blood was drawn for study, it seemed important to discover if there was any effect of surgical operation on the iodoacetate index. It is interesting that several investigators have demonstrated that the plasma fibrinogen and sedimentation rate increase considerably after surgical operations and remain increased above normal for one or 2 weeks. It was demonstrated in this study that surgical operation causes a decrease in the iodoacetate index, which frequently is very pronounced and apparently may persist for at least 2 weeks; for this reason no patients who had had recent surgical operations were included in the compilation and general discussion of the data concerning the effect of cancer and other miscellaneous pathologic conditions on the iodoacetate index.

Huggins has recently reviewed the literature concerning the serum protein concentrations in patients with cancer and has concluded that in most patients with "significant" carcinoma, exclusive of multiple myeloma, the serum albumin and total protein are decreased, the decreases being from moderate to pronounced in patients with late cancer.

Abels and his associates, in a study of the serum proteins in gastrointestinal cancer, found hypoproteinemia of a moderate degree in 29 of 50 patients. This hypoproteinemia was observed to result from decreases in the serum albumin fraction of the serum protein and was attributed in most cases to impaired fabrication of albumin by the liver, rather than to insufficient dietary intake of protein. In the present study, the data on serum total protein and albumin concentrations in normal subjects and in patients with cancer contribute additional information on this point. The finding that 19 of the 51 patients with cancer had serum total protein concentrations below the usual low limit of the authors' normal findings of 6.3 Gm. per 100 cc. demonstrates a tendency toward hypoproteinemia in cancer of various organs. The findings that 11 of 19 patients with gastro-intestinal cancer showed moderate hypoproteinemia accords well with the results of Abels et al. In the 19 patients who had hypoproteinemia, the average protein was 5.9 Gm. per 100 cc. which shows that the degree of hypoproteinemia was not usually great. Furthermore, the studies of serum albumin in a small series of these patients with cancer again demonstrate that when the hypoproteinemia occurs it is attributable to a lowering of the albumin fraction of the total protein.

The finding that the iodoacetate index was frequently abnormally low in patients with malignant tumors, infections, certain ulcerative lesions and other conditions, as well as after surgical procedures, coupled with the fact that the sedimentation rate is also frequently abnormal in these conditions, suggested that there might be some correlation between the results of these 2 measurements. This problem seemed of particular interest, because abnormal results with both these tests have been attributed to change effected by the liver in

the plasma concentrations of fibrinogen when the sedimentation rate is abnormal, and of an albumin fraction when the iodoacetate index is abnormal. Although the corrected sedimentation rate was found to be increased above normal in many patients with abnormally low iodoacetate indexes, it was also found to be normal in a considerable number of patients with low iodoacetate values. Conversely, the corrected sedimentation rate was increased well above the normal in a patient with a normal iodoacetate index. To these observations of no close correlation between the 2 tests, may be added the observation of Huggins et al. that the iodoacetate index is normal in pregnancy, whereas the sedimentation rate is uniformly increased after the third month in pregnancy.

The findings of this study demonstrate that the iodoacetate index test does not constitute a useful tool for the diagnosis of the presence of cancer. (New England J. Med., 25 May '50, D. R. Gilligan et al.)

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Indications for Operations Performed for Cancer of the Distal Colon and Rectum: As a result of studies on the lymphatic spread of carcinoma of the rectum and the large bowel, the author and co-workers have developed certain indications for the type of operation which is to be performed.

Squamous-cell carcinoma of the perianal skin which does not involve the mucosa of the bowel is excised widely and deeply. The defect is closed by turning skin flaps. If the inguinal nodes are enlarged, a radical groin dissection is done on the side of the lesion, or on both sides if the lesion crosses the midline, or if there are enlarged nodes on the opposite side. If the inguinal nodes are not enlarged, they are examined at 2- or 3-month intervals and a radical dissection is performed if any enlargement is noted. When squamous-cell carcinoma of the perianal skin involves the mucosa of the bowel, metastasis will take place upward to lymph nodes along the superior hemorrhoidal artery as well as to the inguinal nodes. In such cases an abdomino-perineal resection is performed, with wide excision of the perianal tissues. The inguinal nodes are treated as previously described.

For adenocarcinoma of the rectum arising from the mucosa and involving the perianal skin, abdominoperineal resection is performed and the inguinal lymph nodes treated as previously described.

Adenocarcinoma of the rectum, which lies entirely or partially below the reflection of the peritoneum from the anterior surface of the rectum to the bladder or uterus, even with the most radical operation, has given a high incidence of local recurrence, by reason of the anatomic relationship of the rectum to the base of the bladder, to the prostate and seminal vessels, or to the uterus and vagina. Direct spread in this location is easy, because there is no peritoneal layer to separate the structures; also, the lymphatic spread is both

upward along the superior hemorrhoidal vessels, and laterally along the lymph vessels on the superior surface of the levator ani muscles. Such lesions may be no more than 6 cm. from the mucocutaneous line, or they may be 12 or 14 cm. away. The anatomic relationship, rather than the distance in centimeters, is the relevant factor. Because of the poor prognosis, the most radical procedure possible is performed; i.e., a Miles type of abdominoperineal resection with division of the superior hemorrhoidal vessels at least 1 and 1/2 inches above the promontory of the sacrum, and the widest possible lateral resection of the levator ani muscles and their accompanying lymphatics.

In cases of carcinoma of the rectum, in which the bowel containing the tumor is completely covered by peritoneum anteriorly, and in which the tumor lies below the promontory of the sacrum, the operative procedure depends upon certain findings. If the lymph nodes along the superior hemorrhoidal vessels are not markedly enlarged, if the tumor is not large, and if there is no fixation to adjacent structures or signs of obstruction, treatment for these lesions is by resection upward as in the first part of an abdominoperineal resection. The bowel and mesentery are examined and if the blood supply seems adequate (which it usually is), an end-to-end anastomosis, usually with a decompressing proximal colostomy, is done. The bowel and mesentery are divided at least 1 and 1/2 inches (or preferably, 2 inches) below the growth. Often an obstruction resection is done, extraperitonealizing the 2-barreled colostomy, as described by David. If the proximal lymph nodes are enlarged and there are signs of lymph-edema and thickening of the bowel wall proximal to the tumor, or if the tumor is adherent to the adjacent structures, then an abdominoperineal resection is done. The mesentery of the rectum and sigmoid are resected just distal to the most proximal palpable artery, which will supply blood to the proximal part of the sigmoid colon. If the tumor is as just described, but the lymph nodes are enlarged proximally to the proposed line of resection of the mesentery, or if it is suspected that the centrally placed lymph nodes may be involved, a frozen section of such nodes may be made to see whether they contain carcinoma. If carcinoma is found in such nodes (with or often without the use of frozen sections), the inferior mesenteric artery is divided at the aorta and the soft parts are dissected downward from the level of the ligament of Treitz, laying bare the aorta and the left ureter and kidney, and removing the descending colon, sigmoid colon, and rectum as described by Rosi. The splenic flexure is then brought out as a terminal colostomy. This is a relatively simple procedure.

For carcinoma of the redundant loop of sigmoid colon, in which there is no fixation to other structures, in which there are very few palpable lymph nodes, and in which there has been little obstruction, resection of the superior hemorrhoidal artery and sigmoid arteries, leaving only one arterial branch to supply the proximal end of the sigmoid or the distal end of the descending colon is carried out. Often the vessels are divided just distally to the left

colic artery. The bowel is mobilized far down in the hollow of the sacrum and is divided at a level where there is a good blood supply coming from the middle and inferior hemorrhoidal vessels. After mobilization of the left colon to the splenic flexure, an end-to-end anastomosis of descending colon to the stump of rectum is performed, usually with a proximal decompressing colostomy. If there is doubt concerning the blood supply to the rectal stump, continuity can be established safely with an extraperitoneal obstruction resection, as described by David.

For carcinoma of the redundant loop of sigmoid, in which there are enlarged nodes and probable lymphatic extension along the origin of the inferior mesenteric artery, treatment is carried out by resection of that artery and stripping of the aorta and left ureter to the level of the ligament of Treitz. The descending colon and sigmoid colon are resected. The gastrocolic omentum is divided, opening the lesser peritoneal cavity and allowing easy mobilization of the splenic flexure, so that it can be joined to the proximal end of the rectum either by end-to-end anastomosis or by obstruction resection.

Carcinomatous lesions may be adherent or fixed. Whenever the tumor has become tightly adherent to another viscus, as the base of the bladder, the uterus, vagina, prostate, seminal vessels, urethra, other loops of bowel, abdominal wall, etc., the patient is given the chance of cure by wide resection of the original tumor and the adherent structure en masse. Forty percent of such a group of patients in whom resection was carried out from 11 to 6 years ago survived the operation more than 5 years, free of any sign of cancer.

The main objective is to remove the cancer. The most radical resection of the regional lymphatics is performed. After this is done, continuity is re-established whenever possible. (Surgery, May '50, Editorial, R. K. Gilchrist)

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In Vivo Coloring of Pelvic Lymph Nodes with India Ink: An in vivo method of coloring the lymph nodes draining the region of the uterine cervix is presented, using India ink solution injected preoperatively. In over 40 patients it consistently caused the nodes to be colored black, and did not discolor any other tissues. The method is presented as an aid to complete removal of all nodes draining the cervix in the Wertheim-type operation for cervical carcinoma, and particularly as an aid in teaching the operation.

The India ink used is an aqueous colloidal suspension of carbon black, being neutral or slightly alkaline in reaction, and containing edible gelatin and shellac gum. Because carbon forms a nonionizing colloid, the particles are picked up almost solely by the lymphatics and deposited in the various nodes along the chain.

The cervix and vaginal vault are prepared with a dry sponge and painted with an aqueous antiseptic. The anterior lip of the cervix is grasped with a single-toothed tenaculum, and 0.5 cc. of autoclaved India ink solution, one part of ink to 2 or 3 parts of sterile distilled water, is injected into the lateral surface of the cervix at 3 and 9 o'clock, the solution being placed just under the mucosa. A tuberculin syringe, because of its small diameter, and a 24-gauge needle are used for the injection. No narcotic or sedative is necessary in most cases, as there is no more pain associated with the procedure than with any hypodermic injection.

This method of injection is the best of several technics tried. A larger volume of ink was used at first, but the larger volume was more painful to inject, and it diffused through so much tissue near the cervix that visualization for dissection became difficult; moreover, the larger volume gave no more intensive coloring of the nodes.

Early in the series the ink was injected into the substance of the cervix with a long 22-gauge needle, but soon a small needle was substituted, and the injection made into the loose connective tissue just under the mucosa.

It was interesting to observe in several of the patients in whom the injection was made on only one side of the cervix that in from 16 to 24 hours the nodes on the side of injection were colored as usual, and the nodes on the opposite side were also colored, although not so intensely. Because the injected mass remains in a small volume of tissue, definitely limited to one side of the cervix, a profuse lymphatic anastomosis across the midline must be present in the cervix.

In all patients on whom the technic was used, the pelvic lymph nodes, including all of the iliac nodes, the obturator nodes, and the lower presacral nodes, were distinctly colored and readily visible after very little dissection of retroperitoneal fat. In one thin patient the nodes over the sacral promontory could be seen through the peritoneum before dissection was started, but this was unusual. The time from injection of the cervix to laparotomy was usually from 16 to 24 hours, with extremes of 4 hours and 42 and 3/4 hours. In those patients who were injected from 16 to 24 hours before surgery, the gross coloring of the nodes was unaffected by time of the menstrual cycle, age of patient, presence of severe chronic pelvic inflammatory disease, or carcinoma in the cervix. As early as 4 hours after injection of the cervix, the obturator and lower iliac and hypogastric nodes may be colored gray, but maximum coloring is apparently obtained after about 8 hours, and is still present after over 40 hours.

In none of the patients was there any gross or microscopic evidence of inflammatory reaction at the site of injection in the cervix. In 7 patients, nodes were sent to the pathology laboratory for study. In only one patient did

the nodes show subacute inflammation, and this was attributed to the chronic inflammatory disease that was present in the pelvis. In no case was the architecture or cellular detail of the node distorted or obscured. The carbon granules in the nodes, which were apparently aggregates of the submicroscopic colloidal particles, were almost all within phagocytic cells which were distributed mainly under the capsule and in the germinal centers, although they could be found almost anywhere in the node. In none of the patients was there discoloration of any tissue other than the nodes and the cervix at the site of injection. (Am. J. Obst. and Gynec., May '50, P. R. Zeit and G. Wilcoxon)

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Air Evacuation of Tuberculous Military Patients: This report is concerned with the immediate and long-range effects of transportation by airplane of 143 military patients having active pulmonary parenchymal tuberculosis in various stages. It is based on a survey initiated in the fall of 1944 as a side mission of the Section for Research on Minimal Tuberculosis. At the time of this study, air-ambulance-planes were not equipped for cabin pressurization at higher altitudes, a desirable feature which has become generally available in more recent years.

Air travel entails high speeds and occasional jolting of the entire body; in nonpressurized airplanes, it also involves sharp changes of altitude with the related changes in barometric pressure and oxygen tension. It is considered that any or all of these factors might affect the course of a chronic infectious disease of the lungs. The present study is concerned only with the immediate and eventual reactions to these factors, rather than with an effort to analyze the potential differential influences of the physical and physiologic components involved.

In an effort to eliminate some of the known variables, such as age, sex, and race, the series was restricted to white males, from 22 to 28 years of age. Prior to evacuation by air, each of the 143 patients had been diagnosed as having active pulmonary tuberculosis, confirmed in practically all instances by sputum or gastric washings positive for Mycobacterium tuberculosis, and had been observed in a distant hospital for at least 2 weeks. At initial preflight diagnosis, the disease had been minimal in 59 instances, moderately advanced in 56, and far advanced in 28, according to the classification standards of the National Tuberculosis Association. Each patient was in flight for 8 hours or more. All patients were followed for at least 3 years.

Each case study was initiated by preliminary direct observation on arrival via air ambulance, followed by full interview within a day or two after deplaning. With very rare exceptions, the air-borne evacuée exhibits less fatigue, less anxiety, more cheerfulness, and higher morale than does the patient who has traveled by train or boat. This statement is substantiated by similar direct observations on hundreds of tuberculous patients arriving via boat or train.

Details concerning the selection of patients for evacuation by airplane, symptoms and objective reactions in flight, duration and maximum altitude of flight, roughness of travel, et cetera, were checked with the medical officers, nurses, and medical corpsmen who accompanied the patients and with the flight crews concerned. Patients with pre-existing therapeutic or spontaneous pneumothorax were not transported by air, nor were the ones with large cavities and associated toxemia. In this group and also among several hundred other tuberculous air evacuees seen more casually , there was no occurrence of spontaneous pneumothorax during or following flight. On the other hand, spontaneous pneumothorax has developed several times among other tuberculous patients being transferred by train to Denver, Colorado, and more often in those crossing Raton Pass by train en route to Santa Fe, New Mexico.

In a very few instances of minimal disease without clinical toxemia, the patients were transferred in an ambulatory status. All others were handled as litter cases, remaining recumbent throughout flight. Flight symptoms, postflight toxemia, and subsequent course of disease were the same for ambulatory and litter patients. Less than one half of the group had previously flown in airplanes.

Severe discomfort, pulmonary hemorrhage, and spontaneous pneumothorax did not occur in the series either during or following flight. Evidences of toxemia appeared or increased immediately after flight in only 3 patients.

The subsequent long-range course of disease was favorable in 128, or 89.5 percent, and unfavorable in 15, or 10.5 percent, of the series. Of the 15 patients whose disease worsened at some time during postflight observation, 4 had been flown at 10,000 feet or less, representing 5.6 percent of the 72 in the lower altitude group; 11 had exceeded 10,000 feet, representing 14.1 percent of the 71 patients who were flown in higher altitudes in nonpressurized airplanes.

The authors conclude that: 1. Almost all military tuberculous patients have expressed a decided preference for transportation by airplane rather than by boat or train.

2. In the absence of contraindications such as very severe toxemia, large cavities, extensive loss of air-bearing lung tissue, or pneumothorax, air travel appears to be safe for tuberculous patients at altitudes up to 10,000 feet, and even preferable to slower modes of transportation.

3. The ultimate influence of flight altitudes above 10,000 feet is difficult to appraise. The experiences of this survey suggest, however, that the eventual course of disease is not as favorable among patients who exceed 10,000 feet in nonpressurized airplanes as among those who are flown at levels below 10,000 feet. (Am. J. Rev. Tuberc., May '50, W. H. Roper and J. J. Waring)

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Blood Sludge Phenomenon in Human Subjects: Knisely has described as "blood sludge," intravascular precipitation and agglutination of red blood cells in fatal malaria and other ominous pathologic conditions. The inference has been made that such intravascular clumping of red cells occurs as a part of a morbid mechanism, that its presence indicates disease, and that it occurs as a prelude to tissue damage. It was the purpose of this study to explore the validity of this inference through observations on a variety of human subjects.

Repeated day to day observations were made on a group of 35 patients with assorted diseases, including carcinoma, acute myocardial infarction, hypertension, pneumonia, pulmonary embolism, and acute rheumatic fever. Also, examinations for sludging were made daily for 10 months on 5 apparently normal healthy subjects. All 5 (3 males and 2 females) were active members of the hospital staff and were free of significant body complaints or known systemic illness. The arterial blood pressure was determined by a sphygmomanometer cuff at the time of observation and records were kept of the occurrence of head colds and minor bodily symptoms among these subjects, and later correlated with the observations on sludging. A diary of events in the day-to-day life situation was recorded, with data on prevailing mood, attitudes, emotions, and feeling states.

A standard American binocular dissecting microscope similar to that illustrated in Knisely's report was used to make direct observations of the blood flow in the scleral and conjunctival vessels of these human subjects. A clear view was thus obtained at a magnification of 30x against the white scleral background. Empty vessel walls and white cells could not be identified at this magnification. The capillaries, venules and arterioles were visible only if they contained blood.

Under circumstances of normal flow the vessels appeared to be of homogeneous red color. Single red cells were not distinguishable. Even in capillaries no particulate matter was seen. The stages of blood sludging were identified as: streaming, i.e., appearance of rapidly and evenly flowing particulate matter and granules along the course of the vessel in which clumps or individual red cells were not distinguishable; and as sludging, i.e., distinguishable clumps of red cells of varying size which flowed slowly, intermittently or not at all. These red cell aggregates were separated by varying amounts of clear plasma.

Among the group of patients with various diseases there was observed in the same individuals wide daily fluctuations in the presence and degree of sludging. No consistent correlation was established between sludging and the clinical state of the individual as measured by symptoms, fever, blood counts or changes in sedimentation rate of the red cells. In some, sludging was never

seen; in others sludging was typical only in the convalescent stage of their illness. When sludging was observed it was frequently not widespread. It was seen to occur occasionally in only one or two vessels, or occasionally in as many as 90 percent of the vessels accessible to view. There was very much variation in the same subject from day to day.

In the long-term observations in normal subjects, great variation in sludging was also recognized. Marked and generalized sludging was repeatedly observed in 4 of the 5 subjects. In the fifth only localized sludge in a small fraction of the vessels was ever noted. These subjects displayed the same degree and variation in the sludging phenomenon as was seen in the group of patients. Often no sludging was seen in any of the vessels. As among the patients it was repeatedly observed that large particles and marked stasis of flow occurred in a few vessels while the remainder of the vascular bed appeared normal.

The red cell aggregates were not consistently associated with furuncles, nasopharyngitis, fever, fluctuations in blood pressure, with variations in life situations and emotional state of the subjects, or with menses.

Stasis at the bifurcations of vessels was often observed, but no vessel spasm or constriction was visible at these points. The column of clumps separated by plasma often halted and then moved on again as a clump moved into a larger stream. In 2 of the healthy subjects, segments of vessels containing packed and stationary clumps were repeatedly observed to remain for as long as 3 days. Thereafter, the "pseudothrombus" disappeared, leaving no visible trace.

The only consistent association observed was that between the degree of sludge and the degree of local vasodilatation in the conjunctiva. At times when many vessels of all sizes were widely visible in the same person, there was more hesitant slow flow of the clumps than when the width and number of vessels was reduced. This finding suggested an alternate interpretation that sludging was a phenomenon of reduced velocity of the stream or of reduced centrifugal force from increased volume of the capillary bed. Thus, it appears that the occurrence of sludging is the result of the slowing of blood flow, rather than the cause of it.

In order to explore further this possibility, 8 patients with marked generalized sludging were given 2 drops of a 10-percent ophthalmic neo-synephrine solution in one eye. Continuous observations were then made during the ensuing rapid vasoconstriction. Arterioles and venules promptly narrowed and many capillaries disappeared entirely within from 20 to 30 minutes. With vasoconstriction the clumps of sludging disappeared in the eyes of 6 subjects and in the other 2 it was greatly diminished, so that only fine particles could be seen

in the larger vessels. Spurting fluid columns were evident in arterioles. In all 8 the opposite untreated control eye showed no change in the amount or degree of blood sludge.

Five subjects without visible sludging were given flushing subcutaneous doses of 1.0 mg. of histamine phosphate. Within 10 minutes there was evident vasodilatation of the conjunctivae with associated widespread sludging. These changes observed following either local neo-synephrine or histamine subsided with 1 or 2 hours.

It is suggested that blood sludging in the conjunctivae is the result of an increase in the volume of the local vascular beds and a decrease in the velocity of blood flow. It is evident, moreover, that widespread sludging in the conjunctival vessels is compatible with good health and well being. (Am. J. M. Sc., May '50, H. S. Robertson et al.)

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A Clinical Evaluation of the Blood Sludge Phenomenon: The purpose of this report is to demonstrate that blood sludging is essentially a reversible intravascular agglutination or clumping phenomenon caused by the same factors which are responsible for a rapid blood sedimentation rate, i.e., the increased rouleaux forming tendency which develops in blood when there are certain changes in plasma proteins and other blood constituents.

Intravascular sludging has been described in the past under other names. The phenomenon commonly occurs in man and other mammals and reflects in a general way the state of health of the individual whose blood is being investigated.

During their studies of the blood sedimentation phenomenon, the authors noted that intravascular agglutination, as described by Fahraeus, did occur in patients with a rapid sedimentation rate. The authors made over 1200 observations of the conjunctival capillary circulation in one year and, in general, found a close correlation between the blood sedimentation rate and the degree of sludging in the capillaries.

A standard Leitz capillary microscope with 15 watt tungsten illumination was used for all the observations. An arbitrary standard of from + to ++++ was established for evaluating the degree of sludging in the capillaries. Although this type of estimation is quite crude, it can nevertheless be significantly informative when practiced by a single observer or a team of observers. After making over 500 preliminary examinations, the authors were able to recognize the maximum amount of sludging in the capillaries, designated as ++++; this appeared as very coarse granular accumulations of erythrocytes separated

from each other by spaces containing clear plasma, with the whole column of blood moving slowly and at times haltingly.

Sedimentation rates were determined by the Westergren method and serum proteins determined by the method of Cohn and Wolfson.

A close correlation was found between the sedimentation rate and the degree of sludging in 82.4 percent of the 619 persons studied. There was a very wide distribution of all types of disorders in this group of patients. All the diseases ordinarily seen in a large general hospital were represented. Investigations were made in all age groups except infants and small children.

The cases were separated into 4 groups of sedimentation rates in order to compare them with the 4 groups representing the degree of sludge formation. The table below records the correlation between the sedimentation rate groups and the degree of sludging.

TABLE 1.—1000 OBSERVATIONS (619 CASES) OF BLOOD SEDIMENTATION RATES CORRELATED WITH THE INTENSITY OF BLOOD SLUDGE FORMATION

Degree of Sludging	*Sedimentation Rates*							
	0–20 mm.		*20–60 mm.*		*60–100 mm.*		*Over 100 mm.*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
0+	123	76.4	36	9.5	7	2.3	0	0
++	18	11.2	249	65.5	22	7.2	15	9.7
+++	19	11.8	63	16.6	249	81.9	38	24.5
++++	1	0.6	32	8.4	26	8.6	102	65.8
Totals	161	100	380	100	304	100	155	100

The group in which there was no correlation between the sedimentation rate and the degree of sludging (17.6 percent) was given further study. This group was separated into 2 groups, cases in which the sludging was less than the sedimentation rate (5.5 percent) and those in which it was greater (12.1 percent).

Rapid blood sedimentation, well developed sludging, and hyperglobulinemia were frequently associated together. Such a concurrence was to be expected because of the strong rouleaux forming properties of the serum globulins. Sludging and rapid sedimentation were frequent in anemic individuals. On the other hand, no sludging and an absence of sedimentation was observed in each of 5 cases of erythrocytosis (polycythemia vera and congenital heart disease).

The authors consider that their observations indicate that the blood sedimentation phenomenon is merely the in vitro manifestation of the process of

sludging in vivo, in agreement with the observations of Fahraeus. It has been known for many years that the phenomenon of erythrocyte sedimentation is a manifestation of Stoke's Law and that increased rouleaux aggregation among the erythrocytes is the immediate cause of the increased rate. Rouleaux aggregation itself is a product of properties of the erythrocyte surface and plasma proteins, particularly fibrinogen and other globulins. Fahraeus and others have demonstrated that the phenomenon occurs in vivo and, when present, results in changes in the stream of circulating blood. Knisely during the last decade observed this phenomenon in malaria and other pathologic conditions. He apparently was not, until recently, familiar with the work of Fahraeus. Because of this, confusion has developed and many clinicians believe that blood sludge is a newly discovered entity of considerable pathologic importance. Knisely insisted that blood sludging differs from intravascular rouleaux aggregation. This may be true in cases of Plasmodium knowlesi malaria in monkeys, but many doubt that sludging in human beings is in any way different from the intravascular rouleaux aggregation of Fahraeus. Knisely has stated that the sludging occurs when a sticky fibrin-like deposit forms on the erythrocytes, causing them to adhere one to another. However, sludge formation is not prevented by heparinization. This should indicate that fibrin does not have a part in the phenomenon.

The rapidity of the circulation in the capillaries depends upon cardiac efficiency and the resistance in the capillaries themselves. Capillary resistance depends upon the viscosity of the blood and tne caliber of the capillaries. Blood viscosity is almost directly proportional to the concentration of the erythrocytes. If clumping of erythrocytes occurs intravascularly and clumps of viscous erythrocytes enter the small capillaries, a slow and interrupted flow develops in those capillaries. Clumping increases because the movement of the circulation is slow. Fragile clumps which form in the larger vessels do not increase in size because of the rapidity of the blood stream. However, in the small capillaries, where there is a slow movement of blood and at times almost complete stasis, contiguous clumps readily adhere to each other and the sludge mass increases in size. Rouleaux aggregation is more intense in anemia because there is more plasma protein in each volume unit of blood to affect the erythrocyte surface. The opposite conditions prevail in erythrocytosis. In heart failure the cardiac output is often reduced and the circulation time is increased. The motion of the circulation is less and sludge formation is protected. This may explain the discrepancy between the sedimentation rates and the degree of sludging in the 40 cases of heart disease which were observed. (Am. J. M. Sc., May '50, J. S. Hirschroeck and M. Woo)

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The Effect of Vasectomy Upon the Incidence of Epididymitis After Prostatectomy: After having performed routine vasectomy for many years as part of the preoperative preparation of patients in whom prostatectomy was contemplated, the authors in 1943 decided to re-evaluate the incidence of epididymitis. Accordingly, the routine use of vasectomy was abandoned. After 2 years, however, it became obvious that the incidence of postoperative epididymitis had risen significantly; vasectomy was therefore resumed as a routine procedure.

Urinary infection (particularly in the presence of residual urine), instrumentation, and the condition of the verumontanum are three important predisposing factors in the cause of epididymitis. Crabtree and Brodny have emphasized the importance of postoperative infection in the prostatic fossa in producing epididymitis and Rathbun considered instrumentation an important predisposing factor; the work of Kreutzmann has put both of these concepts upon a firm footing by demonstrating that cultures of the vas are negative except in cases in which the urine is infected, and that instrumentation doubles the frequency of positive cultures from the vas and hence doubles the possibility of epididymitis. Inflammation of the verumontanum is thought to be necessary for the entry of bacteria into the ejaculatory ducts; congestion of the verumontanum may be predisposing to the entry of bacteria; and direct trauma to the ejaculatory ducts, which frequently occurs in prostatectomy, is also a factor.

Infection may reach the epididymis through the lumen of the vas, through the sheath of the vas, and by the blood stream. The theory of lymphatic transmission has been discarded by most observers. It has been observed on numerous occasions following vasectomy that infection has passed down the vas to the site of interruption but has not affected the epididymis. It is believed that infection commonly passes through the lumen of the vas. The proved value of vasectomy confirms this, and demonstrates that epididymitis caused by blood-borne infection is uncommon.

Postoperative epididymitis is to be avoided because it is a painful condition, and in the older age group in which prostatectomy is mostly performed its disadvantages are more marked than in a younger group. The disadvantages are pain, mental depression and lowered morale, increased susceptibility to other infections, increased danger of thrombophlebitis, atelectasis and pneumonia (because of the patient's increased resistance to ambulation), longer incontinence, postponement of instrumentation, subsequent delay in fistula closure, the possibility of abscess formation or orchitis, the possibility of a local or blood-borne spread of the infection, an increased financial drain on the patient, and a slower hospital turnover. The disadvantages of vasectomy are limited to those associated with any operative wound, and permanent sterility, which in most cases is not significant.

The incidence of postoperative epididymitis has been reported from many clinics. In open prostatectomy, it has varied from 6 percent to 50 percent without vasectomy, and from 0 percent to 4 percent in series in which vasectomy was done; in transurethral prostatectomy it has varied from 1 percent to 8 percent without vasectomy and 2.66 percent following vasectomy; and in transurethral resection with vasoligation, it has been reported as 13.6 percent. Preoperative epididymitis has been reported as 7.58 percent and 11.86 percent. Complications of vasectomy have been reported as varying from 1 percent to 3.5 percent.

In most of the patients concerned in this study, vasectomy was performed either upon entry to the hospital or before cystoscopy was performed (cases in which vasectomy was performed elsewhere are included). Vasectomy should be performed before urethral instrumentation is carried out. The technic of vasectomy includes a high scrotal incision to expose the vas. A segment of vas 1 cm. or more in length is excised. Strict attention is given to aseptic technic.

The present study concerns operations on the prostate performed at the Franklin Hospital in San Francisco by the senior author and associates over a period of 9 years, between 1939 and 1948. The series includes 6 types of operations, namely, transurethral, conservative perineal, radical perineal, suprapubic, retropubic, and perineal biopsy performed on private and clinic patients. Follow-ups were secured on most of these patients for a period of 3 months or longer.

In this study, 810 operations are analyzed. The pathologic changes included benign hypertrophy, median bar, carcinoma, and 1 case each of granuloma and of coincident carcinoma and sarcoma, both apparently primary. In 5 patients radical perineal prostatectomy followed initial transurethral resection. Two-stage transurethral resection cases were listed as one operation; cases in which repeat transurethral resection was necessary after a period of from months to years were listed as separate cases. Antibiotics were used only when specific indication existed and not routinely. With the exception of the two-year period beginning in 1943, vasectomy was performed in the majority of patients. Exceptions were made in men of the younger age groups in whom sterilization was not entirely desirable and in patients who objected to the procedure. Epididymitis had been present in 38 patients in the period up to 2 months prior to hospitalization. Eight of these cases had followed prostatic surgery elsewhere. It occurred in 13 cases within 2 months of surgery, of which 5 cases preceded entry, 2 cases were present upon entry and 6 cases developed during preoperative hospitalization. There were no cases of preoperative epididymitis which followed vasectomy.

A total of 320 vasectomies was done preoperatively, of which roughly 10 percent had been done prior to the hospitalization recorded. A total of 85

patients among the 810 in the study developed epididymitis postoperatively. Of these 85, 12 cases (3.75 percent) followed vasectomy and 73 cases (15.05 percent) occurred among the 490 patients in whom vasectomy was not done.

Inasmuch as there are few figures in the literature giving the incidence of epididymitis following transurethral resection, a separate analysis was made for this operation. Out of a total of 508 cases of transurethral resection, 188 patients had preoperative vasectomy and 320 did not. Of the 188 patients, 5 (2.66 percent) developed postoperative epididymitis; of the 320, 29 (9.06 percent) developed postoperative epididymitis.

The average patient who developed epididymitis following perineal and transurethral prostatectomy spent from 2 to 6 and 1/2 days longer in the hospital than those who did not develop epididymitis.

Nine, or 10.6 percent of the 85 patients with postoperative epididymitis, developed complications. Seven developed scrotal abscesses requiring drainage; one developed bilateral suppurative orchitis, and one developed an acute hydrocele which was drained.

Fourteen patients, or 4.38 percent of the 320 who had preoperative vasectomy, developed complications of this procedure. Wound infection or disruption occurred in 10, hematoma in 2, inguinal abscess in one and a severe dermatitis caused by the skin antiseptic in one. Drainage was necessary in 2 of the cases of wound infection, in one case of hematoma, and in the case of inguinal abscess.

Vasitis or funiculitis developed in 15, or 4.68 percent, of the 320 cases in which vasectomy had been performed. Drainage was necessary in 2 of these. Because it has been demonstrated that infection descends the lumen or the sheath of the vas to the site of interruption, these cases should be considered separately and not as complications of vasectomy. It is probable that, without previous vasectomy, epididymitis would have developed in these cases.

The incidence of epididymitis in this series is in agreement with the reports of Crabtree and Brodny and others who report a significantly lower incidence of epididymitis in open prostatectomy following vasectomy. Lynn and Nesbit report finding no significant difference between two series of 300 cases each of transurethral resection, but have a rather limited number of cases of epididymitis. Nesbit has resumed vasectomy as a part of his preoperative preparation.

Statistical analysis of the figures in this series showed a highly significant difference between the patients having had vasectomy and those not.

Certain factors which are considered important in affecting the incidence of epididymitis are: the amount and type of instrumentation preceding vasectomy, careful cleansing of the urethra as a preliminary to instrumentation, urinary infection, the presence of residual urine both pre- and postoperatively, aseptic vasectomy, and surgical trauma to the verumontanum and to the ejaculatory ducts (which are occasionally cut in transurethral resection).

The authors do not believe that the routine use of sulfonamides is advisable in an attempt to prevent epididymitis in cases in which other indications for their use are lacking; vasectomy performed before initial instrumentation and adequate drainage of infected urine, both pre- and postoperatively, is considered to be of greater importance.

It is concluded from this series that preoperative vasectomy is of significant value in preventing epididymitis following both open prostatectomy and transurethral resection. Vasectomy should be a part of the preoperative preparation of patients in whom prostatic surgery is contemplated. An exception may be made in the younger age group or in patients objecting to the procedure, but the increased risk of epididymitis must be acknowledged. (J. Urol., May '50, S. S. Schmidt and F. Hinman)

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Studies on Airsickness: The sequential results of a series of investigations on the prevention of airsickness, including a preliminary study of the effect of dramamine on the prevention of swing sickness, are presented. The authors state that no attempt is made to appraise the parts played by various physiologic and psychic mechanisms in the production of motion sickness, but the working hypothesis outlined by Campbell is used, i.e., motion sickness is caused by a summation in the central nervous system of stimuli from the vestibular apparatus, the optic apparatus, peripheral kinesthetic receptors (skin, muscle, and joint), visceral receptors, and the psychosoma. It is recognized that in some cases a sufficient stimulation of one of these sensory fields is sufficient to produce symptoms.

Seasickness and airsickness both fall into the symptom complex of motion sickness, and both are true forms of it. However, there is a great difference in the characteristics of the motion stimuli in each type. Seasickness usually occurs as a result of motion which begins mildly and increases gradually in intensity; whereas motion in aircraft is usually precipitated quite suddenly and increases from none to considerable over a period of seconds or minutes, rather than over a period of hours as in seasickness. In addition, the motion encountered in airsickness is usually more abrupt, more violent, more irregular and of greater amplitude than in seasickness. The motion of ships and boats tends to be rhythmical and to follow a pattern in many instances.

Thus, many of the swings and other similar devices which employ rhythmical and regular motion to produce motion sickness experimentally seem to show a higher correlation with seasickness than with airsickness.

In order to test the effectiveness of dramamine in the prevention of airsickness, actual aircraft flights in a C-47 (DC-3) type aircraft with simulated aberrant motion were used. Pilots attempted to simulate flight through turbulence by maneuvering the controls. It was agreed by all concerned that airsickness could be produced by this method, and the resemblance to motion encountered in turbulent air was similar. Although the abrupt pitching and ascending caused by updrafts and downdrafts could not be exactly duplicated, the other components of aircraft motion in turbulence were almost identical. A new and hitherto unused method of producing stimuli capable of causing bona fide airsickness was thus developed. It was felt, moreover, that by conducting tests in aircraft in flight some light might be shed on the role played by psychological factors, such as apprehension and inherent fear of flying in motion sickness. Pending specific studies, the authors are inclined to feel that airsickness is produced by a combination of factors, psychological, physical, and physiological, with no clear evidence indicating which is paramount.

One-hour flights simulating flight through turbulent air in a C-47 (DC-3) airplane were utilized. Volunteers were obtained from among individuals stationed at Randolph Air Force Base who were not on flying duty. No other selection factors were utilized, because it was desired to have as a test group a cross section of young adult males who had not become conditioned or adapted to aircraft motion. On each flight, conditions encountered in flying through gentle and moderately turbulent air were simulated. All variable factors were either controlled or randomized.

As in previous studies carried out on motion sickness at the School of Aviation Medicine, the incidence of airsickness in the subjects was judged on a purely objective basis, i.e., whether or not vomiting occurred. Twelve flights were made, and a total of 216 subjects were tested. One half of the subjects received dramamine and the other half a placebo.

Of those given dramamine, 28.7 percent became ill, as opposed to 55.6 percent among those given a placebo. The rather high sickness rate in the placebo group, which was reduced to almost one half by 100 mg. doses of dramamine, indicated that this compound is a very effective preventive of airsickness. Because several investigators, all working separately, had previously reported hyoscine to be the best drug yet tried, it was decided to compare dramamine and hyoscine in preventing motion sickness, and particularly airsickness. It had previously been found, in repeated experiments, that subjects susceptible to swing sickness were protected to a considerable degree

by hyoscine hydrobromide. Accordingly, it was decided to test the effectiveness of dramamine on swing sickness. A preliminary study of 20 susceptible subjects suggests that dramamine is no more effective than a placebo in preventing swing sickness (only 2 of 10 subjects were protected in each case).

The drugs were also compared in the course of additional studies in aircraft. A series of flights were carried out with half of the subjects receiving 0.65 mg. of hyoscine hydrobromide and the other half receiving 100 mg. of dramamine. In 10 flights, using a total of 176 subjects, dramamine showed a sickness rate of 33 percent, whereas in the first series the rate was 28.7 percent. The subjects who received hyoscine hydrobromide showed a sickness rate of 20.4 percent. Expressed in terms of protection, dramamine in the second series of flights protected 67 percent of all individuals, whereas hyoscine hydrobromide protected 79.6 percent of all individuals. A statistical analysis of these results indicates that if there were no difference in the effectiveness of hyoscine and dramamine, a difference of the magnitude observed could be expected to occur only about six times in 100. In the total of 196 subjects tested in flight, to whom dramamine was administered, the average protection rate was 69.4 percent, compared with the hyoscine protection rate of 79.6 percent, a 10.2 percent difference in favor of hyoscine hydrobromide.

Because dramamine appears to be at most no more effective in airsickness than hyoscine hydrobromide, it is logical to weigh certain other comparable factors. Any preventive of motion sickness if used by airborne troops or aircrew members must not have side effects which might impair the operational efficiency of such personnel as navigators, radio operators, flight engineers, et cetera. Because one of the pharmacologic actions of dramamine is that of a central nervous system depressant, the profundity of this action needed to be assessed. The Civil Aeronautics Administration has recently reported that this drug produced undesirable side effects in a number of instances. Of the 206 individuals given dramamine as a motion sickness preventive, only 18 (8.7 percent) have exhibited significant side effects. These side effects were either one or more of the following symptoms listed in order of frequency of occurrence: (1) extreme drowsiness, (2) mental depression, (3) dizziness. The Department of Psychology at the USAF School of Aviation Medicine conducted a study to determine whether a considerable portion of these symptoms might have been caused in part by the motion stimuli.

A complex coordination test and a reaction time test were used on 2 groups of subjects. The results obtained show no statistical difference between the performances of the control and of the treatment groups and it is, therefore, concluded that dramamine does not significantly affect coordination or reaction time as measured by the testing devices used.

Hyoscine hydrobromide has been studied exhaustively for possible side effects, and this drug, in moderate doses, from 0.65 to 0.75 mg., has been

found to be relatively free from undesirable side effects. Observations by the authors on the group of 88 subjects studied who were given 0.65 mg. doses of hyoscine as an airsickness preventive disclosed no deleterious symptoms except mild dryness of the mouth in 14 cases (15 percent).

Additional studies are being conducted at the USAF School of Aviation Medicine concerning the effectiveness of the antihistaminic group of drugs on motion sickness. Further comparisons of their effectiveness with hyoscine are planned. The Department of Pharmacology is conducting extensive studies of the side effects of dramamine and other antihistaminics.

Summary. The authors of the present study state that the observations on the symptoms of motion sickness have left the impression that the terms vagotonia and sympatheticotonia which have been applied to this condition are actually rarely applicable. No such distinct differentiation in symptomatology was noted among 485 persons subjected to motion stimuli. They consider dramamine (B-dimethylamino-ethyl benzohydryl ether 8-chlorotheophyllinate) to be a very effective preventive of airsickness. Based upon this study, dramamine appears not to be any more effective than a placebo in preventing swing sickness. Hyoscine hydrobromide in doses of 0.65 mg. prevented experimentally produced airsickness in from 10 to 12 percent more subjects than did dramamine. Among 206 persons given 100 mg. doses of dramamine there occurred an 8.7 percent incidence of undesirable side effects. With 0.65 mg. doses of hyoscine hydrobromide the only undesirable side effect noted among 88 persons was dryness of the mouth which occurred in 15 percent. In a controlled study on 30 persons, dramamine did not adversely affect the performance of a complex coordination test or a reaction time test. (J. Aviation Med., April '50, B. A. Strickland, Jr. et al.)

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The Detoxification of DDT by Resistant Houseflies and Inhibition of This Process by Piperonyl Cyclonene: It has been found by numerous experimenters that the common housefly (Musca domestica) becomes less susceptible to the toxic action of DDT after one or more season's exposure. The marked increase in effectiveness of pyrethrin solutions when various so-called synergists are added has led to the hope that synergists might be found for DDT.

A study of several synergists for pyrethrin showed that piperonyl cyclohexenone (piperonyl cyclonene) markedly increases the toxicity of DDT for the DDT-resistant strains of houseflies, but has little or no effect on the ordinary susceptible strain when acetone solutions are applied topically. Preliminary results with DDD and with methoxychlor show similar effects.

Mortalities among the 3 strains of flies used in the experiment were obtained by applying the chemicals together in acetone solution and hence might

be interpreted as resulting from more rapid or complete penetration of the integument by DDT when the synergist was present. This is not the case, because separate application to different parts of the body resulted in the same increase in mortality. In fact, larger amounts used jointly appear to retard penetration and to decrease mortality of the Berkeley strain. Hence, an explanation was sought in changes undergone by DDT after absorption.

Twenty-four hours after application the flies were thoroughly rinsed in chloroform to remove adhering DDT and then were ground and again extracted with chloroform. DDT was determined colorimetrically by the Schechter-Haller method. In some instances a reddish color was produced in addition to the customary blue color. This is an indication of some degradation product, e.g., the acetic acid derivative (DDA), the ethylene derivative (DDE) or perhaps dichlorobenzophenone. The substance giving this color appears not to be removed by dilute alkali and hence the simplest assumption is that it is the ethylene derivative DDE.

An increased ability to convert absorbed DDT into DDE was found to be a characteristic of the resistant strain. In a given experiment, the survivors on the average always had converted more DDT than those that died; the ability to make this conversion is thus interpreted as a major factor in variation in resistance within individuals of a given strain.

Similar analyses on flies that had been treated with the DDT-piperonyl cyclonene combination showed that the conversion to DDE is largely prevented. The synergism is, therefore, at least in part, an interference with the detoxification process. That DDE is not the only decomposition product formed in some cases is indicated by attempts to account for all applied DDT. With survivors from the resistant strains, the sum of external DDT, internal DDT, internal DDE calculated back to DDT, plus these compounds excreted or brushed off in the container usually was at least a third less than the amount of DDT originally applied. The conversion of absorbed DDT to DDE may be an enzymatic process, for flies first killed by heating in air at 80° C. for a few minutes absorbed large amounts of DDT but converted none to DDE.

Work on this problem is continuing. (Science, 2 June '50, A. S. Perry and W. M. Hoskins)

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Thinning Zinc Oxide-Eugenol Dental Impression Pastes: It is often desirable to prepare a thinner mix of zinc oxide-eugenol impression paste than that which is obtained by using the prescribed ratios for the base and the accelerator. The common practice has been to add vaseline or to increase the proportion of the accelerator. These methods produce a thinner mix, but the

final surface of the set impression is soft, crumbly, and easily distorted.

A new method for preparing a thinner mix has been devised; 5 or 6 drops of eugenol are spatulated into the base before adding the accelerator. This will give the desired consistency, and will set with a hard, durable surface that will not become distorted in laboratory handling. The indiscriminate addition of eugenol is contraindicated, because this oil irritates the oral tissues; however, the use of 5 or 6 drops, as described in this method, in the first 15 cases in which the method has been employed, has caused no discomfort to the patients. (H. R. Superko, LCDR, DC, USN, U. S. Naval Dental School, NNMC, Bethesda, Maryland)

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The Possibility of Biological Effects of Cosmic Rays in High Altitudes, Stratosphere and Space: In recent discussions on aeromedical problems of space travel, attention has been called to the possibility that cosmic rays in the stratosphere and in space may influence stratosphere planes, rockets, space ships, and their freight (human beings, animals, and plants).

It has been shown that cosmic radiation under special conditions, especially by secondary effects (shower-formation), can produce biological effects. Not only the primary radiation and the ionization concern the investigator, but also new effects connected with nuclear evaporation processes and nuclear break-up events are encountered, which, in turn, are able to affect biological material.

Cosmic ray research has recently produced new discoveries concerning heavy nuclei in the primary component of cosmic radiation, the creation of high energy cosmic ray stars, the production of mesons, and the origin of the radiation. A review of the present knowledge concerning the possibility of biological effects caused by cosmic radiation at high altitudes and in space seems justified, and necessary in light of the seriousness of aeromedical problems of space travel.

Through the use of these recent discoveries in cosmic ray physics (heavy nuclei in the primary radiation, evaporation and explosion stars) and the present knowledge of the biological effects of cosmic rays, the author shows in his report that at the altitudes considered biological effects of cosmic radiation have to be expected. By comparing the cosmic ray events in high altitudes with data obtained in radium poisoning investigations, an estimation of the magnitude of cosmic ray effects is made. The author recommends that, in order to obtain deeper insight and experience in this field, the following should be investigated:

1. Biological effects of fission processes.

2. General biological effects of exposure of drosophila, seeds, fungi, and protein solutions in extremely high altitudes.

3. Deep mine investigations correlated with 1 and 2 above. (Proj. No. 6-64-12-08-(7), 28 April '50, Medical Dept. Field Research Lab., Fort Knox, Kentucky, A. T. Krebs)

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Navy Offers 200 Hospital Internships to 1951 Medical School Graduates: The Bureau of Medicine and Surgery has announced that 200 rotating internships in U. S. Naval Hospitals will be available to qualified medical school students who will graduate in 1951.

Applications for the naval internships will be accepted beginning on 19 December 1950, in accordance with the Asscciation of American Medical Colleges' cooperative plan for appointment of interns. However, an intern in the U. S. Navy must meet all requirements for commission in the Medical Corps of the U. S. Naval Reserve and it is necessary, therefore, that applications for Naval Reserve commissions be submitted prior to the December date.

Prospective applicants for internships should visit the Naval Officer Procurement Office nearest their homes as soon as possible and apply for a Naval Reserve commission, so that this application may be processed well in advance of 20 February 1951, the deadline for notification of successful internship candidates.

All internship candidates will be notified of their selection or nonselection for the program. Selected candidates will be notified by telegram not earlier than 20 February 1951. At the same time, they will be notified of the naval hospital to which they will be assigned for their intern year. Candidates not selected for an internship in the Navy for any reason will be notified of their nonselection as early as practical after review of their applications, irrespective of date, in order that they may apply elsewhere for an internship appointment prior to the concluding date of the appointment schedule.

Candidates for naval internship are selected from volunteers who agree to serve a minimum of 24 months of active duty from the date of commencement of their intern training. Appointees are commissioned as a lieutenant (junior grade) in the Medical Corps of the Naval Reserve. On graduation from medical school they receive the pay and allowance of their rank while serving as interns. When ordered to other duty upon completion of internship, they also qualify for an additional compensation of $100 per month.

Other benefits include a $250 uniform allowance, reimbursement of transportation cost for dependents and household effects from their home to station of duty, retirement benefits, and an opportunity for later advanced professional training.

Applications and further information concerning the program may be obtained from any Office of Naval Officer Procurement, or by writing to the Personnel Division, Bureau of Medicine and Surgery, Navy Department, Washington 25, D. C.

Naval Officer Procurement offices are located in: Atlanta, Georgia; Boston, Massachusetts; Chicago, Illinois; Cincinnati, Ohio; Dallas, Texas; Denver, Colorado; Detroit, Michigan; Kansas City, Missouri; Los Angeles, California; Minneapolis, Minnesota; New Orleans, Louisiana; New York, New York; Philadelphia, Pennsylvania; Pittsburgh, Pennsylvania; San Francisco, California; Seattle, Washington; Washington, D. C.; and Pearl Harbor, T. H. (Professional Div., BuMed)

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Course in Aviation Medicine for Volunteer Naval Reserve Medical Officers: A course of instruction for inactive Reserve medical officers holding the designation of flight surgeon or aviation medical examiner has been established at the Naval School of Aviation Medicine, U. S. Naval Air Station, Pensacola, Florida from 10 July 1950 to 22 July 1950 inclusive.

The purpose of this course is to provide Reserve flight surgeons and aviation medical examiners with information on advances in aviation medicine which would not be available to them in their civilian capacity. This information would be invaluable to their function in the event of mobilization.

Only the 1st, 3rd, 4th, 5th, 6th, 8th, and 9th Naval Districts, the Potomac River Naval Command, and the Chief of Naval Air Reserve Training have been assigned a quota for this course.

Inactive Volunteer Reserve medical officers with the designation of flight surgeon or aviation medical examiner residing in the above mentioned naval districts, who desire to attend this course, should submit their request for training duty to the commandant of their local naval district at the earliest practicable date. Meals and sleeping quarters will be available at the bachelor officers' quarters for those who desire such accommodations.

It is anticipated that two additional similar courses in aviation medicine will be convened some time during the fiscal year which begins 1 July 1950. The dates for these two other courses, when set, will be announced. (Reserve Div., BuMed)

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Course in Amphibious Medicine for Volunteer Naval Reserve Medical Officers: A course of instruction for inactive Volunteer Reserve medical officers has been established at the Amphibious Training Command, Naval Amphibious Base, Little Creek, Virginia from 10 July 1950 to 22 July 1950 inclusive.

The purpose of this course is to familiarize Reserve medical officers with amphibious operations in general and the medical aspects thereof in particular. The course will present material designed to give medical officers an appreciation of the complexities of the amphibious operation and the need for careful and thorough planning to handle the medical problems that arise during such an operation.

In order to keep within the optimum age grouping for training in amphibious medicine, it is planned to nominate only medical officers in the grade of lieutenant (junior grade) and lieutenant for this course. Only the 1st, 3rd, 4th, 5th, 6th, 7th, 8th, and 9th Naval Districts and the Potomac River Naval Command have been assigned a quota for this course.

Inactive Reserve medical officers residing in the above naval districts who desire to attend this course should submit their request for training duty to the commandant of their local naval district at the earliest practicable date. Meals and sleeping quarters will be available at the bachelor officers' quarters for those officers who desire such accommodations.

It is anticipated that two additional courses in amphibious medicine will be conducted at a later date. (Reserve Div., BuMed)

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Training Program for Naval Reserve Entomologists and Malariology Technicians: It is planned to conduct training courses of two weeks in duration for Naval Reserve entomologists and malariology technicians at the Navy Malaria and Mosquito Control Unit No. 1, U. S. Naval Air Station, Jacksonville, Flo[illegible]a during the fiscal year which begins 1 July 1950, classes to convene on the first and third Wednesday of each month.

These courses will provide an opportunity for Reserve personnel to receive two weeks of annual training duty. The latest information concerning the needs, methods, and operations of insect and pest control workers will be presented in each course.

Inactive Naval Reserve ent[illegible]ologists and malariology technicians residing in the 1st, 3rd, 4th, 5th, 6th, 8th, and 9th Naval Districts and the Potomac River Naval Command who desire to perform this annual training duty should submit a request to the commandant of their local naval district. (Reserve Div., BuMed)

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Advanced Medical Training in Radiological Defense: Announcement has been made by the Armed Forces Special Weapons Project of an advanced medical training course in radiological defense to be given at Duke University Training Center, Durham, N. C. The didactic training period will commence on or about 1 September 1950 and will be of five months' duration. This phase of the instruction will be followed by three months of on-the-job training at an installation of the Atomic Energy Commission.

Requests are desired immediately from medical officers of the regular Navy who are interested in this field of study. In accordance with BuPers Circular Letter 49-50 of 7 April 1950, each request for this course must contain an agreement to serve on active duty for a period of three years, which includes the time covered by this instruction. Requests may be made by dispatch if the time element involved requires such action. Dispatch requests must be confirmed by a following letter. Requests must reach BuMed before 15 July 1950 to receive consideration. (Professional Div., BuMed)

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SECNAV LETTER Op24C/cj, Serial 205P24 28 April 1950

To: All Ships and Stations

Subj: Disestablishment of U. S. Naval Medical Supply Depot, Brooklyn, N. Y.; Establishment of U. S. Naval Medical Supply Depot, Edgewater, N. J.

1. The following activity is hereby established under a commanding officer:

U. S. Naval Medical Supply Depot
River Road
Edgewater, New Jersey 4200-407

This activity is under the military command and coordination control of the Commandant, Third Naval District, and under the management control of the Bureau of Medicine and Surgery. It includes all the physical facilities of the Medical Supply Depot Annex, Edgewater, New Jersey.

2. The following activity is hereby disestablished:

U. S. Naval Medical Supply Depot
Sands and Pearl Sts.
Brooklyn 1, New York 4200-400

Concurrent with the disestablishment, the physical facilities of the foregoing activity will comprise an annex of the U. S. Naval Supply Depot, Edgewater, New Jersey, but will not be designated as a separate activity of the Navy.

3. Holders of Basic Naval Establishment Plan, Fiscal Year 1950, after entry of Change No. 1, correct paragraph 7220 to read as follows:

7220 - U. S. Naval Medical Supply Depot, Edgewater, N. J. (Includes Brooklyn Annex, Brooklyn, New York.)

4. Bureaus and offices concerned take necessary action.

--SecNav. Francis P. Matthews.

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SECNAV LETTER Op24C/cj, Serial 479P24, 28 April 1950

To: All Ships and Stations

Subj: Establishment of Biological Laboratory, Naval Supply Center, Oakland, Calif.

1. The following activity is established effective 1 January 1950, under an officer in charge:

U. S. Naval Biological Laboratory
Naval Supply Center
Oakland, California 3860-600

This activity is under the military command and coordination control of the Commander, U. S. Naval Base, San Francisco, exercised through the Commanding Officer, U. S. Naval Supply Center, Oakland, California, and under the management control of the Office of Naval Research.

2. Holders of the Basic Naval Establishment Plan, Fiscal Year 1950, add the following paragraphs:

6705 U. S. Naval Biological Laboratory,
Naval Supply Center, Oakland, California

6705a Mission - Conduct research on air-borne infectious diseases and the behavior of the agents of these diseases.

3. Bureaus and offices concerned take necessary action.

--SecNav. Francis P. Matthews.

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BUMED CIRCULAR LETTER 50-55 26 May 1950

From: Chief, Bureau of Medicine and Surgery
To: Commandants, All Naval Districts (less 10, 15, and 17)
Commandant, Potomac River Naval Command
Commanding Officer, NMSD, River Road, Edgewater, N. J.
Commanding Officer, NMSD, Oakland, Calif.

Subj: Medical Allowances for Naval Reserve Training Activities (less Aviation) - Modifications to

Ref: (a) BuMed Circular Letter No. 49-115, as modified by C.L. No. 49-153

This letter deletes 9 stock numbers from the present list and replaces them with 9 new stock numbers. Requisitions may be resubmitted with new stock numbers in cases of cancellation from requisitions of deleted old stock numbers. Because the deleted item is an authorized substitute for the new item, the new item is not to be requisitioned if the deleted item is on hand.

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BUMED CIRCULAR LETTER 50-56 Joint Letter 26 May 1950

From: Chief of Naval Personnel
Chief of the Bureau of Medicine and Surgery
To: Commandants, All Naval Districts and River Commands

Subj: Officers' Fitness Reports for Medical and Dental Officers and Ensigns (HP) Undergoing Professional or Technical Training or Courses in Civilian Institutions; Submission of

Refs: (a) Art. 1701, U. S. Navy Regulations, 1948
(b) Arts. B-2202 and H-1810, BuPers Manual, 1948
(c) BuMed-BuPers Joint Ltr., BuMed-31-nlj, P20-2/OM, BuMed C/L No. 49-78; BuPers-P20-2(a), Pers-8232-rdf, of 16 June 1949

This BuPers-BuMed joint letter cancels reference (c). Fitness reports should indicate that subject officers are under instruction. Addressees should obtain from the civilian institution a letter giving an appraisal of the officer's progress for use in making out the fitness report. If appropriate, the letter may be appended to the report. A copy of the letter, in each case, shall be forwarded to BuMed, attention Code 3 for medical officers, and Code 6 for dental officers.

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BUMED CIRCULAR LETTER 50-57 31 May 1950

From: Chief of the Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Naval Aviation Selection Tests; Revised Forms and Procedures Concerning

Refs: (a) BUMED Circular ltr No. 49-37 of 1 Apr 1949
(b) BUMED Circular ltr No. 44-82 of 15 May 1944
(c) BUMED Circular ltr No. 46-153 of 15 Oct 1946
(d) BUMED Circular ltr No. 48-83 of 28 July 1948
(e) Joint Letter BuMed - BuPers, BUMED Circular ltr No. 44-45, of 15 Mar 1944
(f) Joint Letter BuMed - BuPers, BUMED Circular ltr No. 48-118, of 5 Nov 1948

A copy of this letter appears in the 31 May 1950 Navy Department Bulletin. References (a), (b), (c), and (d) are canceled as of 1 July 1950.

The new forms for the Aviation Classification Test (ACT) and the Mechanical Comprehension Test (MCT) are being supplied in accordance with information supplied BuMed in response to reference (a). The flight surgeon or aviation medical examiner, if attached, shall be directly responsible for the security, administration, and forwarding of these tests. The scoring and recording will, in the future, be done in BuMed. The superseded material shall be destroyed in accordance with current regulations. Answer sheets which are not to be folded or mailed in the same envelope with Form 68 are to be sent to BuMed upon completion. Activities not responding to reference (a) but responsible for administration of subject tests and requiring a supply should make request to BuMed.

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NAVY DEPARTMENT
BUREAU OF MEDICINE AND SURGERY
WASHINGTON 25, D. C.

OFFICIAL BUSINESS

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